Therapeutic Results after the Introduction of Tailored CAS

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Objective: We examined whether the introduction of tailored carotid artery stenting (CAS) was effective for the prevention of periprocedural ischemic complications.

Methods: In patients who underwent CAS, we compared the incidence of new ischemic lesions on postprocedural diffusion weighted image (DWI) and periprocedural ischemic stroke between three periods: the early period when primarily distal balloon protection was used, the intermediate period when primarily distal filter protection was used, and the late period after the introduction of tailored CAS.

Results: CAS was performed in 16 lesions in the early period, 30 lesions in the intermediate period, and 69 lesions in the late period. New ischemic lesions on postprocedural DWI were detected in 1 (6.3%), 6 (20.0%), and 12 (17.4%), respectively. Periprocedural ischemic stroke occurred in three lesions (10%) during the intermediate period, but did not occur during the early and late periods.

Conclusion: The incidence of new ischemic lesion on DWI did not change even after the introduction of tailored CAS, but no periprocedural ischemic stroke occurred, suggesting that tailored CAS is effective for its prevention.

Keywords ▶ carotid artery stenting, ischemic complication, unstable plaque

Introduction

Carotid artery stenting (CAS) was approved in Japan in 2008, but periprocedural ischemic complications have been reported to occur more frequently in CAS than in carotid endarterectomy (CEA), and they must be reduced to improve the safety of CAS.¹⁾ We report that the incidence of periprocedural ischemic complications was reduced by the introduction of tailored CAS, in which the therapeutic strategy is changed according to the results of evaluation of plaque characteristics.

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Methods

The subjects were 108 patients (115 lesions) who underwent CAS at our facility between August 2003 and July 2016 with a mean age of 72.7 years (range: 55–90 years). Males accounted for 85.2% of the patients, 60 lesions were symptomatic, and the mean percent stenosis was 75.9% (**Table 1**). MRI was performed on the day after treatment in all patients except one with a pacemaker. The existence and number of new ischemic lesions were examined by diffusion weighted image (DWI). The de novo neurologic deficits that appeared during the procedure, ipsilateral cerebral infarction (including asymptomatic lesions) within 1 month and 1 year after treatment, and postprocedural restenosis (area stenosis $\geq 50\%$ and peak systolic velocity ≥ 200 cm/sec by carotid ultrasound) were also evaluated.

The patients were divided into three groups according to the period in which CAS was performed: the early period (August 2003–January 2008), when primarily Guardwire plus 300 cm (Medtronic, Minneapolis, NM, USA) was used for distal embolic protection, the intermediate period (February 2008–February 2010), when primarily Angioguard XP (Cordis, Johnson & Johnson, Miami, FL, USA) was

Table 1 Patient profile and treatment periods

N	115 lesions (108 patients)
Age, years, mean (range)	72.7 (55–90)
Males, n (%)	98 (82.5)
Symptomatic lesions, n (%)	60 (52.2)
Stenosis rate, %, mean (range)	75.9 (36.6–99)
Vulnerable plaques, n (%)	22 (19.1%)
Treatment period	
Early (August 2003–January 2008)	16 lesions
Intermediate (February 2008–February 2010)	30 lesions
Late (March 2010–July 2016)	69 lesions

used, and the late period (March 2013–July 2016) after the introduction of tailored CAS, in which the device was selected based on the evaluation of plaque characteristics.

Plaque characteristics of carotid artery stenotic lesions were examined, and plaques that met any of the following were defined as vulnerable plaques: 1) hypoechoic or mobile plaque on carotid ultrasonography, 2) those with a plaque/sternocleidomastoid muscle signal intensity ratio of ≥ 1.25 on T1-weighted black-blood (BB) MRI,²⁾ and 3) those showing white plaque sign on time-of-flight (TOF) MRA.³⁾

In tailored CAS, the flow reversal technique to induce reflux in the internal carotid artery by occluding the common and external carotid arteries was used for vulnerable plaques (Group P), distal balloon protection was used when flow reversal was technically impossible or when the plaque was not judged to be vulnerable (Group B), and distal filter protection was used for patients who did not tolerate temporary obstruction of the internal carotid artery such as patients with contralateral internal carotid artery occlusion (Group F). In Group P, flow reversal was induced using 9F OPTIMO (Tokai Medical Products, Aichi, Japan) or 9F Cello (Medtronic) as a balloon guiding catheter and Carotid GuardWire (Medtronic) for external carotid artery occlusion, and the reversed blood flow was returned to a 4F sheath placed in the contralateral inguinal femoral vein via a transfusion filter. Carotid GuardWire was used in Group B, and Angioguard XP (Cordis, Johnson & Johnson) or Filterwire EZ (Boston Scientific, Natick, MA, USA) was used in Group F, as a distal embolic protection device. Closed-cell stents were selected except for tortuous or markedly calcified lesions, for which open-cell stents were used. We used Precise (Cordis, Johnson & Johnson) or Protégé (Medtronic) as an open-cell stent and Carotid Wallstent (Boston Scientific) as a closed-cell stent.

Results

The 115 lesions consisted of 16, 30, and 69 lesions treated in the early, intermediate, and late periods, respectively.

Of these lesions, a diagnosis of vulnerable plaque was made preprocedurally in 1 (6.3%), 2 (6.7%), and 19 (27.5%), new ischemic lesions were detected on postprocedural DWI in 1 (6.3%), 6 (20.0%), and 12 (17.4%), periprocedural ischemic stroke was observed in 0, 3 (10.0%), and 0, restenosis was observed in 1 (6.3%), 4 (13.3%), and 1 (1.5%), and ipsilateral cerebral infarction was observed within 1 year in 0, 1 (3.3%), and 3 (4.3%), respectively (**Table 2**).

By the protection device, 54 lesions were classified as Group B, 33 lesions as Group F, and 28 lesions as Group P. Of these lesions, new ischemic lesions were detected on postprocedural DWI in 7 (13.0%), 7 (21.2%), and 5 (17.9%), intraprocedural ischemic symptoms were observed in 1 (1.9%), 4 (12.1%), and 0, periprocedural ischemic stroke was occurred in 1 (1.9%), 2 (6.1%), and 0, and ipsilateral cerebral infarction occurred within 1 year in 2 (3.8%), 2 (6.1%), and 0, respectively (**Table 3**).

Discussion

According to the time of treatment, periprocedural ischemic stroke was less frequent in the early and late periods although the differences were not significant. Particularly, in the late period, many patients had vulnerable plaques, but no perioperative ischemic stroke was observed probably because of the introduction of tailored CAS. In this period, flow reversal was selected aggressively as a measure to prevent intraprocedural embolism due to vulnerable plaques. Parodi et al. reported that flow reversal, aimed to prevent distal embolism by reversing the blood flow at the site of stenosis, was theoretically the safest method for distal embolic protection.⁴⁾ Initially, it was necessary to use 10.5F OPTIMO as a balloon guiding catheter, but 9F OPTIMO and 9F Cello, which is 0.090" in internal diameter, became usable, and options were increased by the advent of Mo-Ma Ultra (Medtronic). In some cases, however, the superior thyroid artery is anatomically located near the bifurcation of the carotid artery, and the antegrade blood flow from the superior thyroid artery

Table 2 Treatment results in various periods

	Total number	Vulnerable plaques	DWI positive	Mean No. of DWI-positive lesions	Peri-CAS ischemic stroke	Post-CAS restenosis	Ipsilateral infarction within 1 year
Early period	16	1 (6.3%)	1 (6.3%)	1	0	1 (6.3%)	0
Group B	16	1	1 (6.3%)	1	0	1 (6.3%)	0
Group F	0	0	0	0	0	0	0
Group P	0	0	0	0	0	0	0
Intermediate period	30	2 (6.7%)	6 (20.0%)	10.2	3 (10.0%)	4 (13.3%)	1 (3.3%)
Group B	9	1	2 (22.2%)	12.5	1 (11.1%)	1 (11.1%)	0
Group F	20	1	4 (20.0%)	9	2 (10.0%)	3 (15.0%)	1 (5.0%)
Group P	1	0	0	0	0	0	0
Late period	69	19 (27.5%)	12 (17.4%)	2.3	0	1 (1.5%)	3 (4.3%)
Group B	29	8	4 (13.8%)	2.5	0	1 (3.4%)	2 (6.9%)
Group F	13	2	3 (23.1%)	2.7	0	0	1 (7.7%)
Group P	27	9	5 (18.5%)	2	0	0	0

CAS: carotid artery stenting; DWI: diffusion weighted image

Table 3 Treatment results by the protection device

	Total number	DWI positive	Intraprocedural ischemic symptoms	Periprocedural ischemic stroke	Ipsilateral infarction within 1 year
Group B	54	7 (13.0%)	1 (1.9%)	1 (1.9%)	2 (3.8%)
Group F	33	7 (21.2%)	4 (12.1%)	2 (6.1%)	2 (6.1%)
Group P	28	5 (17.9%)	0	0	0

DWI: diffusion weighted image

to the internal carotid artery persists via collaterals despite occlusion of the common carotid artery and external carotid artery. We, therefore, make sure to check reversal of the flow of the internal carotid artery by angiography or carotid ultrasonography. In our patients, flow reversal of the internal carotid artery could not be achieved in 5 (14.7%) of the 34 patients in whom the procedure was attempted, and it was necessary to change the distal embolic protection method. The complexity of the procedure is considered to pose no major problems once the therapist becomes accustomed to it. Concerning hemostasis of the puncture site, we presently replace the sheath with a 4F sheath, etc., and perform hemostasis by manual compression for 10 minutes, followed by the application of 8F Angio-Seal (TERUMO, Tokyo, Japan) or 7F Exoseal (Cordis, Johnson & Johnson). Although we have encountered no complications, the advent of hemostatic devices compatible to 9F catheters is awaited.

In the intermediate period, the outcomes of not only ischemic complications but also restenosis and ipsilateral cerebral infarction within 1 year were poor. While vulnerable plaques were observed in about 6% of the patients in both the early and intermediate periods, there is a possibility that the outcomes in the intermediate period were exacerbated due to underestimation of the frequency of vulnerable plaques in those days as the signal intensity

ratio could not be quantified by preprocedural BB imaging, a rapid increase in the number of cases with approval of CAS in Japan, and a decline in the learning curve associated with the introduction of new filter type devices. These experiences prompted our understanding about plaques, more strict and robust checks for vulnerable plaques, evaluation of measures for distal embolic protection, and use of the aggressive medical treatments such as statins, cilostazol, and eicosapentaenoic acid (EPA) preparations and led to the introduction of tailored CAS.

During the late period after the introduction of tailored CAS, the incidence of new ischemic lesions by postprocedural DWI increased compared with the early period (6.3% → 17.4%) and did not change markedly compared with the intermediate period (20.0% → 17.4%). However, the fact that the DWI findings were primarily multiple/scattered positive lesions (mean number: 10.2) in the intermediate period but mostly isolated lesions (mean number: 2.3) in the late period is considered to have contributed to the decrease in periprocedural ischemic stroke (10.0% → 0%).

Regarding the periprocedural aggressive medical treatment, dual-antiplatelet therapy (DAPT) was performed in all patients, and it was combined with cilostazol for the prevention of intraprocedural bradycardia and restenosis in some patients.^{5,6)} Concerning statins, also, rosuvastatin

5 mg or atorvastatin 10 mg was administered to high-low-density lipoprotein (LDL) cases, and fluvastatin 30 mg, pravastatin 10 mg, or pitavastatin 2 mg was administered appropriately also to normal-LDL cases, in expectation of plaque stabilization.⁷⁾ Fatty acid fraction analysis began to be covered by healthcare insurance during the late period, and we administered ethyl-eicosapentaenoic acid at 900 mg twice a day or omega-3 acid ethyl ester at 2 g a day, also in expectation of plaque stabilization.⁸⁾ These medications might contribute to the decrease in periprocedural ischemic complications.

However, ipsilateral cerebral infarction occurred after the periprocedural period despite these aggressive medical treatments. These events, which were free of troubles such as in-stent thrombosis and occurred irrespective of the time of discontinuation of DAPT (3–12 months after treatment), are problems to be addressed in the future.

Conclusion

The results of CAS have improved by preprocedural diagnosis of plaque characteristics and appropriate selection of the distal embolic protection method. For the future, it is necessary to explore solutions for ipsilateral cerebral infarction occurring within 1 year.

Disclosure Statement

Neither the first author nor any of the coauthors have any conflicts of interest.

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